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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/590,419	08/15/2008	William W. Bachovchin	TUV-048.01	7018

25181 7590 09/27/2010  
FOLEY HOAG, LLP  
PATENT GROUP, WORLD TRADE CENTER WEST  
155 SEAPORT BLVD  
BOSTON, MA 02110

EXAMINER
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PIHONAK, SARAH

ART UNIT	PAPER NUMBER
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1627

NOTIFICATION DATE	DELIVERY MODE
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09/27/2010

ELECTRONIC

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

Patent@foleyhoag.com

<b>Office Action Summary</b>	<b>Application No.</b> 10/590,419	<b>Applicant(s)</b> BACHOVCHIN ET AL.	
	<b>Examiner</b> SARAH PIHONAK	<b>Art Unit</b> 1627	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 04 August 2010.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1 and 3-16 is/are pending in the application.
- 4a) Of the above claim(s) 8-12, 15 and 16 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1, 3-7, 13 and 14 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)          | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____                                      |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)          | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____  | 6) <input type="checkbox"/> Other: _____                          |

### **DETAILED ACTION**

This application is a national stage entry of PCT/US05/06127, filed on 2/23/2005.

### **Priority**

This application claims priority from Provisional Application No. 60/547226, filed on 2/23/2004.

### **Response to Remarks**

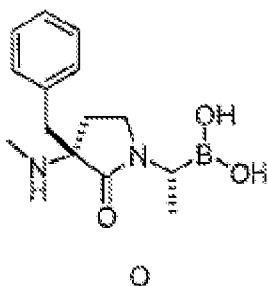
Previously, claims 1-16 were pending, with claims 8-9, 10-12, and 15-16 withdrawn due to the restriction requirement. In the reply filed on 8/4/2010, the Applicants cancelled claim 2. Currently, claims 1, 3-7, and 13-14 are under active examination; claims 8-9, 10-12, and 15-16 remain withdrawn from consideration.

Applicant's arguments, with respect to the rejections under 35 USC 102(b) as being anticipated by Scheidt et. al., Gianessi et. al., and Natchev have been fully considered and are found persuasive. The claims have been amended to further limit R<sup>6</sup>; due to the claim amendments, the rejections under 35 USC 102(b) as being anticipated by Scheidt et. al., Gianessi et. al., and Natchev are withdrawn.

Applicant's arguments, with respect to the rejection under 35 USC 103(a) have been fully considered and are found persuasive. Due to the claim amendments, this rejection is withdrawn.

Applicants have further defined the variable 'L' in the claims; therefore, due to the claim amendments, the rejection under 35 USC 112, second paragraph is withdrawn. In further consideration of the amended claims, new rejections have been made, which will be discussed in detail in the office action. Accordingly, this action is made FINAL.

1. As noted by the examiner in the office action dated 3/4/2010, the Applicants have defined the variables L, X, Y, and R<sup>1</sup> as being either absent or present with the claimed substituents. Additionally, in the specification, the Applicants have named exemplary structures of the invention as including the compound shown below (p. 23 of specification):



For this compound, the amine group is substituted by methyl. However, Y is not defined as being an alkyl group. The only variable that includes an alkyl group is L or R<sup>1</sup>. Therefore, it has been interpreted by the examiner that if Y or X are absent, the acyclic nitrogen can have a direct bond with either L or R<sup>1</sup>.

2. Claims 1, 3-7, and 13-14 were examined.
3. Claims 1, 3-7, 13, and 14 are rejected.

### Claim Rejections-35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application

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by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

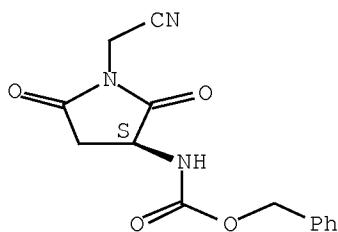
5. Claims 1 and 4-7 are rejected under 35 U.S.C. 102(e) as being anticipated by Thomas et. al., WO 2004/022536 (filed in English on 9/3/2003).

The claims are directed to a compound as defined by formula I.

Thomas et. al. discloses a claimed compound of formula I, shown below (p. 40, intermediate 9, lines 1-18):

IT 672883-17-9P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);  
RACT  
(Reactant or reagent)  
(intermediate; preparation of heterocyclic amides, in particular  
azolanes  
and pyridines, as Phosphodiesterase IV (PDE4) inhibitors for  
treatment  
of inflammatory and allergic disorders)  
RN 672883-17-9 HCAPLUS  
CN Carbamic acid, [(3S)-1-(cyanomethyl)-2,5-dioxo-3-pyrrolidinyl]-,  
phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



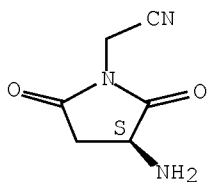
Where, as defined by formula I, n=0; L on ring A is absent; R<sup>7</sup>=oxo on ring A; R<sup>4</sup>, R<sup>5</sup>=H; R<sup>6</sup>=CN; R<sup>3</sup>=H; R<sup>2</sup>=H; Y=C(O); X=-O-; L=-CH<sub>2</sub>-; R<sup>1</sup>=phenyl.

Thomas et. al. also discloses the claimed compound of formula I, shown below

(p. 58, lines 7-10, preparation of (3S)-3-amino-1-cyanomethylazolan-2,5-dione):

IT 672883-37-3, (3S)-3-Amino-1-cyanomethylazolan-2,5-dione  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(preparation of heterocyclic amides, in particular azolanes and pyridines,  
as Phosphodiesterase IV (PDE4) inhibitors for treatment of inflammatory  
and allergic disorders)  
RN 672883-37-3 HCAPLUS  
CN 1-Pyrrolidineacetonitrile, 3-amino-2,5-dioxo-, (3S)- (CA INDEX NAME)

Absolute stereochemistry.



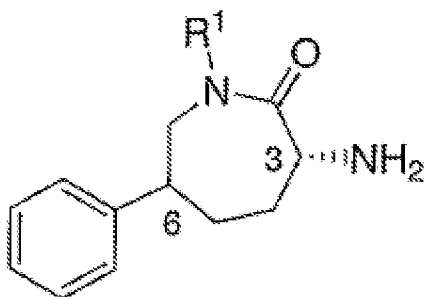
Where, as defined by formula I, R<sup>4</sup>, R<sup>5</sup>=H; L of ring A is absent; R<sup>7</sup>=oxo on ring A; R<sup>3</sup>=H; R<sup>2</sup>=H; Y, X, L=absent; R<sup>1</sup>=H. While Thomas et. al. does not disclose that the compounds are protease inhibitors, are orally active in a mammal, or inhibit dipeptidyl peptidase IV with a K<sub>i</sub> of 50 nM or less, such characteristics are properties of these compounds. A compound and its properties are not patentably distinct; See M.P.E.P.

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2141.02, *In re Papesch*, 315 F.2d 381, 391, 137 USPQ 43, 51 (CCPA 1963). Thomas et. al. also discloses the compound in a pharmaceutically acceptable solvent, such as methanol (p. 58, lines 7-10); therefore, Thomas et. al. discloses the compound in a pharmaceutical composition, and anticipates the claims.

**6. Claims 1 and 4-6 are rejected under 35 U.S.C. 102(e) as being anticipated by Burgey et. al., WO 2004/092168 (priority filing date 4/15/2003).**

Burgey et. al. discloses the following claimed compound of formula I (p. 29, Table I-1, intermediate compound 10):



Where  $R^1 = \text{CH}_2\text{CN}$ . The compound is defined by formula I as follows:  $n=2$ ; L of ring A is absent;  $R^7$  is attached directly to ring A and is phenyl;  $R^3 = \text{H}$ ;  $R^2 = \text{H}$ ; X, Y, and L are absent;  $R^1 = \text{H}$ . While Burgey et. al. does not disclose that the compound is a protease inhibitor, orally active in a mammal, or inhibits dipeptidyl peptidase IV with a  $K_i$  of 50 nM or less, such characteristics are properties of this compound. A compound and its properties are not patentably distinct; See M.P.E.P. 2141.02, *In re Papesch*, 315 F.2d 381, 391, 137 USPQ 43, 51 (CCPA 1963). Therefore, as Burgey et. al. discloses the claimed compound of formula I, Burgey et. al. anticipates the claims.

### **Claim Rejections-35 USC § 103**

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

8. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

9. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

10. Claims 13 and 14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Thomas et. al., WO 2004/022536, as applied to claims 1 and 4-7 above, and

further in view of Remington's: the Science and Practice of Pharmacy, 19<sup>th</sup> edition, vol. 1, p. 806 (of previous record).

As discussed supra, Thomas et. al. discloses compounds of formula (I), as well as the compound in a pharmaceutically acceptable solvent.

Thomas et. al. does not teach a packaged pharmaceutical, comprising preparation of a compound with instruction describing the use of the preparation.

Remington's teaches that the labeling of pharmaceuticals, along with instructions for preparation of the pharmaceutical for prescription and usage is a requirement by law, under 21 CFR 201.57 (p. 806, left column, 4<sup>th</sup> full paragraph-right column, all paragraphs). The ability to inhibit a post-proline cleaving enzyme, as well as to regulate glucose metabolism, are properties of the claimed compounds. Therefore, as Remington's teaches that proper labeling and descriptive information of pharmaceuticals, as well as instructions for use are a requirement by law, it would have been prima facie obvious for one of ordinary skill in the art, at the time of the invention, to include information along with the pharmaceutical with instructions for the preparation of inhibiting a post-proline cleaving enzyme, and for regulating glucose metabolism. Additionally, packaging of the pharmaceutical would have been considered a part of labeling and providing descriptive information and instructions for the drug compounds.

### **Claim Rejections-35 USC § 112**

11. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

12. Claim 3 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 1 recites the limitation that  $R^6$  is selected from the group consisting of cyano, boronic acid,  $-SO_2Z^1$ ,  $P(=O)Z^1$ ,  $-C(=NH)NH_2$ ; and  $-CH=NR^{12}$ ; claim 3, which is a dependent claim of claim 1, cites that  $R^6$  is a group of  $B(Y^1)(Y^2)$ , wherein  $Y^1$  and  $Y^2$  are independently OH or a group hydrolysable to OH, or together with the boron atom to which they are attached form a 5- to 8-membered ring that is hydrolysable to boronic acid. As claim 1 cites that  $R^6$  is boronic acid, but does not cite that  $R^6$  can be groups which are hydrolysable to boronic acid, there is insufficient antecedent basis for this limitation in claim 3.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

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the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

### **Conclusion**

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SARAH PIHONAK whose telephone number is (571)270-7710. The examiner can normally be reached on Monday-Thursday 8:00 AM - 6:30 PM EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on (571)272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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S.P.

/SREENI PADMANABHAN/

Supervisory Patent Examiner, Art Unit 1627